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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,872	04/05/2001	Alan Solomon	044137-5029-US	3133

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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
KAM, CHIH MIN	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 03/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/825,872	SOLOMON ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,32-34,37-55 and 57-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 32-34, 37-55 and 57-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-3, 32-34, 37-55 and 57-68 are pending.

Applicants' amendment filed December 23, 2005 is acknowledged. Applicants' response has been fully considered. Claims 1, 37, 50, 57-59 and 63 have been amended, claims 35, 36 and 56 have been cancelled, and new claims 64-68 have been amended. Therefore, claims 1-3, 32-34, 37-55 and 57-68 are examined.

Withdrawn Informalities

2. The previous objection to the specification regarding citing an amino acid sequence without providing the "SEQ ID NO:" and sequence listing, is withdrawn in view of applicants' submission of sequence listing and computer readable form, and applicants' response at page 8 of the amendment filed December 23, 2005. CRF has been entered.

Withdrawn Claim Rejections - 35 USC § 102

3. The previous rejection of claims 1, 2, 32-45, 50-52, 56-61 and 63 under 35 U.S.C. 102(e) as being anticipated by Schenk (U.S. Patent 6,875,434), is withdrawn in view of applicants' amendment to the claims, and applicants' response at pages 11-12 of the amendment filed December 23, 2005.

4. The previous rejection of claims 1, 32-45, 56, 57 and 59 under 35 U.S.C. 102(a) as being anticipated by Schenk (WO 99/27944), is withdrawn in view of applicants' amendment to the claims, and applicants' response at pages 11-12 of the amendment filed December 23, 2005.

Claim Objections

5. Claim 37 is objected to because of the citation of the term "32-microglobulin" and "amyloid 3 –protein". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 32-34, 37-55 and 57-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of removing amyloid deposits from a subject comprising administering to the subject a specific amyloid fibrils such as synthetic fibrils composed of an immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide homologous to the amyloid fibrils in the subject in an effective amount to generate an immune response, wherein the immune response promotes the removal of amyloid deposits from the subject; or a pharmaceutical composition formulated for removing amyloid deposits from a subject comprising specific amyloid fibrils homologous to the amyloid fibrils in the subject, does not reasonably provide enablement for a method of removing amyloid deposits from a subject comprising administering to the subject amyloid fibrils, or amyloid fibrils comprising an immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide heterologous to the amyloid fibrils in the subject in an effective amount to generate an immune response, wherein the immune response promotes the removal of amyloid deposits from the subject; or a pharmaceutical composition formulated for removing amyloid deposits from a subject comprising amyloid fibrils heterologous to the amyloid fibrils in the subject; a

vaccine composition comprising amyloid fibrils or a whole immunoglobulin light chain polypeptide; or a method of removing amyloid deposits from a subject comprising administering to the subject the vaccine composition comprising amyloid fibrils. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 1-3, 32-34, 37-55 and 57-68 are directed to a method of removing amyloid deposits from a subject comprising administering to the subject amyloid fibrils, or amyloid fibrils comprising an immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide heterologous to the amyloid fibrils in the subject in an effective amount to generate an immune response (claims 1, 2, 32-34, 37-45, 50-52, 57, 58 and 63); or a pharmaceutical composition formulated for removing amyloid deposits from a subject comprising amyloid fibrils heterologous to the amyloid fibrils in the subject (claims 59-61, and 65-68); a vaccine composition comprising amyloid fibrils or a whole immunoglobulin light chain polypeptide (claims 3, 46-49, 53-55, 62); or a method of removing amyloid deposits from a subject comprising administering to the subject the vaccine composition (claim 64). The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the present invention provides a method of removing amyloid deposits from a patient, comprising administering amyloid fibrils to generate an immune response that will promote the removal of in vivo amyloid fibrils; and also provides a vaccine or pharmaceutical composition comprising an amyloid fibril and a carrier (page 10, paragraph [0035]). There are no indicia that the present application enables the full scope of the claims in view of the use of a vaccine or pharmaceutical composition comprising amyloid fibrils in the method of removing amyloid

deposits from a subject as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding various amyloid fibrils contained in a pharmaceutical or a vaccine composition used in the method of removing amyloid deposits from a subject, which is not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The specification has demonstrated the use of a pharmaceutical composition containing immunoglobulin light chain variable region in the method of removing amyloid fibrils in mice with AL-amyloidoma (paragraphs [0128]-[0131]), it has not demonstrated the pharmaceutical composition has removed amyloid fibrils in mice with AA-amyloidosis (immunoglobulin light chain heterologous to AA-amyloid fibrils), or the composition is used as a vaccine to prevent the occurring of amyloid deposits.

(3). The state of the prior art and relative skill of those in the art:

The related art indicates the use of a pharmaceutical composition comprising amyloid fibril components (e.g., amyloid-β peptide or its variants, homologous to amyloid fibrils of the patient) in the method of treating patients suffering from amyloidogenic disease to induce immune response against amyloid deposits in the patient (Schenk *et al.*, WO 99/27944), however, the art does not indicate the use of the composition as a vaccine, nor discloses the use of amyloid fibril components which are heterologous to amyloid fibrils of the patient in the treatment. Thus, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the use and the effect of a composition comprising amyloid fibrils heterologous to amyloid fibrils of the patient in the treatment, or, a vaccine comprising amyloid fibrils and its protective effects for removing amyloid deposits in the patient to be considered enabling.

(4). Predictability or unpredictability of the art:

The claims encompass a method of removing amyloid deposits from a subject comprising administering to the subject amyloid fibrils heterologous to the amyloid fibrils in the subject in an effective amount to generate an immune response; a pharmaceutical composition formulated for removing amyloid deposits from a subject comprising amyloid fibrils heterologous to the amyloid fibrils in the subject; a vaccine composition comprising amyloid fibrils; or a method of removing amyloid deposits from a subject comprising administering to the subject the vaccine composition. While the specification indicates the use of a pharmaceutical composition containing immunoglobulin light chain variable region in the method of removing amyloid fibrils in mice with AL-amyloidoma (paragraphs [0128]-[0131]), it has not demonstrated the pharmaceutical composition has removed amyloid fibrils in mice with AA-amyloidosis

(immunoglobulin light chain heterologous to AA-amyloid fibrils). The specification has not demonstrated the protective effects of a vaccine comprising amyloid fibrils in a subject. Therefore, the invention is highly unpredictable regarding the protective effects of the composition as a vaccine.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of removing amyloid deposits from a subject comprising administering to the subject amyloid fibrils heterologous to the amyloid fibrils in the subject in an effective amount to generate an immune response; a pharmaceutical composition formulated for removing amyloid deposits from a subject comprising amyloid fibrils heterologous to the amyloid fibrils in the subject; a vaccine composition comprising amyloid fibrils; or a method of removing amyloid deposits from a subject comprising administering to the subject the vaccine composition. The specification indicates amyloid fibril encompasses fibrils of immunoglobulin light chain, amyloid A protein, beta 2-microglobulin, transthyretin, cystatin C variant, gelsolin, procalcitonin, PrP protein, amyloid beta-protein, ApoA, lysozyme, variants thereof or allelic variants thereof (paragraph 0078), and the use of a pharmaceutical composition containing immunoglobulin light chain variable region in the method of removing amyloid fibrils in mice with AL-amyloidoma (paragraphs [0128]-[0131]), it has not demonstrated the pharmaceutical composition has removed amyloid fibrils in mice with AA-amyloidosis (immunoglobulin light chain heterologous to AA-amyloid fibrils). Furthermore, it does not show the composition as a vaccine to prevent the occurring of amyloid deposits, and there are no working examples demonstrating the protective effects of a composition containing amyloid

fibrils. Since the specification fails to provide sufficient teaching on the use of a pharmaceutical composition comprising amyloid fibrils heterologous to amyloid fibrils of the subject in the method of removing amyloid deposits, or protective effect of a vaccine composition, it requires undue experimentation to assess the effect of the composition containing amyloid fibrils in a subject.

(6). Nature of the Invention

The scope of the claims encompasses a pharmaceutical composition comprising amyloid fibrils heterologous to amyloid fibrils of the subject in the method removing amyloid deposits, or a vaccine composition comprising amyloid fibrils, but the specification has not demonstrated the effect of amyloid fibrils heterologous to amyloid fibrils of the subject in the method of removing amyloid deposits, nor has shown the protective effects of a vaccine composition comprising various amyloid fibrils in a subject. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed variants and associated methods, the outcome is unpredictable regarding the effects of various amyloid fibrils, and the teachings in the specification are limited, therefore, it requires undue experimentation to assess the effect of a pharmaceutical or vaccine composition containing amyloid fibrils heterologous to amyloid fibrils of the subject.

Response to Arguments

Applicants indicate the specification fully enables the vaccine compositions comprising amyloid fibrils in view of the Wands factors discussed. The claims are directed to vaccine compositions comprising amyloid fibrils. Vaccine compositions comprising amyloid fibrils are

sufficiently described and disclosed in the specification, and paragraphs 0073 to 0089 and 0128-0133 teach how to make and use vaccine compositions. The specification enables the breadth of the claims. The presently claimed vaccine compositions comprising amyloid fibrils have been shown to remove undesirable amyloid deposits from mice (see Example D, page 35 of the specification; and attached reference Hrncic et al. (2001) Amyloid and Amyloidosis, pp.234-235). Many vaccines have been developed for treating diseases, e.g., polio, rubeola and Hepatitis B. Vaccines are being developed for treating neurodegenerative diseases such as Alzheimer's disease (see attached Lambert et al. and press releases from Neurochem). Therefore, the specification enables the claimed invention (pages 8-11 of the response).

The response has been considered, however, the argument is not fully persuasive because of the following reasons. According to the definition of vaccine, vaccine is primarily used to prevent the disease, in the press releases from Neurochem (provided by applicants), which indicates a novel vaccine being developed intended to prevent the development and the progression of Alzheimer's disease, it is clear the vaccine is for preventing a disease to occur. Furthermore, the specification merely demonstrates the use of a pharmaceutical composition containing specific amyloid fibrils (e.g., immunoglobulin light chain variable region) homologous to the amyloid deposits in AL-amyloidoma (paragraphs [0128]-[0131]), it does not show the composition is used as a vaccine to prevent the occurring of amyloid deposits. Thus, it requires undue experimentation to assess the protective effect of the composition containing amyloid fibrils in a subject. Regarding Hrncic et al. (December 2001) Amyloid and Amyloidosis, pp.234-235), which is a post-filing reference and indicates the administration of synthetic light chain fibrils to mice, in which Alκ or ALλ amyloidomas were induced, is found to

accelerate AL amyloidolysis, the reference demonstrates the use of synthetic light chain fibrils in the treatment of amyloidomas, not in the prevention. Therefore, the composition comprising amyloid fibrils as a vaccine composition is not enabled.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CHIH-MIN KAM
PATENT EXAMINER

CMK
March 11, 2006